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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,662	03/01/2004	David J. Chaplin	18217-519 (OXI-19)	9569

30623 7590 11/07/2007

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EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
11/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,662	CHAPLIN DAVID	
	Examiner	Art Unit	
	Timothy E. Betton	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *17-33 and 43-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,34-42 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 pages, 4 June 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse in the reply filed on 3 July 2007 is acknowledged. Also, applicant's Amendments to the Specification disclosing the corrected chemical structure for 2', 3' dihydroxy-4'-methoxy-3, 4,5-trifluoro- (Z)-stilbene (ZSB-71) has been filed and made of record.

Restriction/ Election of Species

In response to the Restriction Requirement mailed June 6, 2007, Applicants elect the invention of Group I, drawn to claims 1-16, 34-42, and 57. Claims 17-33 and 43-56 have been withdrawn. Applicants elect the compound 2', 3' dihydroxy-4'-methoxy-3, 4,5-trifluoro- (Z)-stilbene.

Status of the Claims

Claims 1-57 are pending in the application. Claims 17-33 and 43-56 have been withdrawn. Claims 1-16, 34 –42, and 57 are under examination.

Claim Rejection-35 USC 112, 1ST paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 34-42, and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The instant specification does not reasonably provide enablement due to the absence of any embodiments or representative examples drawn to any direction as to how to make the compound ZSB-71.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Exparte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The state of the prior art requires routine experimentation. Bioactivation of quinone-containing anticancer agents has been studied extensively within the context of the chemistry and structure of the individual quinines, which may result in various mechanisms of activity (Gutierrez, P. L., "The role of NAD(P)H oxidoreductase (DT-diaphorase) in the bioactivation of quinone-containing antitumor agents: a review", Free Radic. Biol. Med., 29(3-4): 263-275 (2000), page 263, 2nd paragraph [already of record]). However, without actual, let alone sufficient support in the instant specification as to how ZSB-71 may be prepared, would make it instantly apparent to the skilled artisan that undue experimentation would prevail at the expense of routine experimentation.

The present invention is directed to a composition which selectively reduces blood flow to a tumor region and forms a reactive oxygen species R-OS in vivo, wherein said composition comprises an anticancer agent having a quinone, quinone prodrug, catechol or catechol prodrug moiety, provided that said composition is not combretastatin A-1 or a salt, ester or prodrug thereof (see claim 1). More specifically, the claimed quinone species is ZSB-71.

In view of this, one of ordinary skill in the art would not be adequately apprised of how to practice the claimed subject matter without a level of undue experimentation because the one of ordinary skill could not sufficiently accept on its face that ZSB-71 could be made due to the absence of any disclosure of such within the instant specification.

As set forth in In re Marzocchi et al., 169 USPQ 367 (CCPA 197 I):

"[A] [s]pecification disclosure which contains tile teachings of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112, unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support." assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling."

The present claims indicate the use and administration of the presently claimed ZSB-71. Likewise, it is noted that the instant specification cites examples directed to the processes of making of other quinone moieties with the exception of ZSB-71. In light of this fact, the specification fails to provide the skilled artisan with any direction or guidance as to how such objectives could actually be achieved, i.e., the process of making ZSB-71. The present specification is viewed as lacking an enabling disclosure of the entire scope of the claimed invention.

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction by Applicant would be undue. Please reference in re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but

whether, *if experimentation is necessary, it is undue".*

In view of the discussion of each of the factors as discussed, the level of skill in the art is high and is at least that of a practicing physician with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the objective directed to treatment with ZSB-71 could be achieved. This is essentially the case due to the absence of representative models in how to make ZSB-71. In order to actually achieve such a result, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the presently claimed invention.

In view of predictability, the instant specification discloses no operative direction as to how to make the claimed compound. If the applicant is claiming a certain species within a genus of instant invention, applicant must disclose how to make such a specific compound for its use in claimed invention. The central issue of a subject claimed pharmaceutical composition or chemical compound is an adequate description, explanation, or analysis of how to make such compounds and compositions.

Additionally, there are exemplified or reasonably representative set of methods which could likewise be reasonably modified by the skilled chemist in such a way as to direct best practices in the embodying art of pharmacy technology via due experimentation.

Working examples are not required, however proper direction in how to make is necessary. Without embodiments directed toward making the claimed compound, unpredictability is high in regard to enablement of subject invention. The quantity of due experimentation would be reasonably expected by one of ordinary skill in the art if there was an adequate description and/or explanation in how to make the claimed chemical compound ZSB-71. The objective outcome of such an invention is not predictable in view of the absence of embodiments directed to ZSB-71 providing guidance in how to prepare said chemical compound.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic
Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H. Marschel 11/4/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

TEB